Brief Communication Communication brève

A retrospective analysis of the epidural use of bupivacaine 0.0625–0.125% with opioids in bitches undergoing cesarean section

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Abstract — Epidural anesthesia, often used during cesarean surgery, can exacerbate hypotension from general anesthesia and delay discharge due to motor block. Decreasing the local anesthetic dose might reduce those complications. Cases of dogs undergoing cesarean section that were anesthetized without epidural ($n = 29$) (control) and dogs with low-dose epidural bupivacaine with fentanyl or buprenorphine ($n = 37$) were reviewed. The incidence of hypotension was equal between groups. Intraoperative opioids were administered more to control (93%) than to treated dogs (18%; $P < 0.0001$). Epidural bupivacaine 0.0625–0.125% combined with an opioid reduced the use of intraoperative opioids and did not exacerbate arterial hypotension during cesarean section in anesthetized dogs.

Résumé — Analyse rétrospective de l'utilisation de bupivacaine 0,0625-0,125 % avec des opioïdes lors d'épidurale chez des chiennes soumises à une césarienne. L'anesthésie épidurale, souvent utilisée lors d'une césarienne, peut exacerber l'hypotension due à l'anesthésie générale et retarder le congé à cause d'un bloc moteur. Une diminution de la dose d'anesthésique local pourrait réduire ces complications. Une revue fut effectuée des cas de chiennes soumises à une césarienne et anesthésiées sans épidurale ($n = 29$) (témoin) et des chiennes avec une épidurale en utilisant une faible dose de bupivacaine avec du fentanyl ou de la buprenorphine ($n = 37$). L'incidence d'hypotension était égale entre les groupes. Des opioïdes intra-opératoires furent administrés plus fréquemment chez les témoins (93 %) que chez les animaux traités (18 %; $P < 0,001$). De la bupivacaine 0,0625-0,125 % en épidurale combinée à un opioïde réduisit l'utilisation d'opioïdes intra-opératoires et n'a pas exacerbé l'hypotension artérielle durant la césarienne chez des chiennes anesthésiées.

(Traduit par Dr Serge Messier)

Epidural anesthesia has long been used to facilitate cesarean section in dogs (1). Its use in sedated dogs was associated with improved puppy vigor when compared with inhalational anesthesia alone (2). In a more recent study, the combination of epidural lidocaine in dogs receiving propofol resulted in a larger percentage of puppies with higher Apgar scores immediately after delivery, than when the epidural lidocaine was not used. However, epidural anesthesia also resulted in lower intraoperative arterial blood pressure (3).

Data on the use of combined epidural and inhalational anesthesia for cesarean section in dogs is scarce. This combination can have potential benefits and disadvantages. Epidural anesthesia can reduce the use of inhalational anesthetics (4) and systemic analgesics (5), but it could result in sympathetic

and motor block, which could promote arterial hypotension or delay discharge until ambulation is resumed (6). These complications might be minimized by reducing the dose of the local anesthetic administered epidurally. Epidural anesthesia with low concentrations of local anesthetics is often used to alleviate labor pain in women while minimizing motor deficits (7). While the low dose of the local anesthetic is not expected to fully abolish nociception, its analgesic efficacy has been well-demonstrated in women.

To evaluate the use of low-dose epidural bupivacaine combined with inhalational anesthesia, cases of canine cesarean sections from 2014 to 2018 in our hospital were retrospectively analyzed. It was hypothesized that i) dogs receiving low-dose epidural anesthesia would require lower doses of general inhalational anesthetics and systemic opioids than those not receiving an epidural anesthetic; and ii) that arterial hypotension would not occur more often in dogs receiving epidural anesthesia.

Medical records of dogs undergoing cesarean section between January 1, 2014 and July 1, 2018 were examined. Records of dogs that did not receive epidural anesthesia (control group) and those that received an epidural injection of bupivacaine at a concentration ≤ 0.125% were included for analysis. All dogs were anesthetized under the supervision of 1 of 4 attending anesthesiologists. Records were excluded if the concentration of

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Table 1. Median (IQR) age, weight, and percentage of dogs with signs of active labor admitted for cesarean between January 2014 and July 2018. Dogs in the epidural group received bupivacaine 0.0625–0.125% with either fentanyl or buprenorphine.

	Epidural	Control	P-value
Weight (kg)	29 (22.7 to 34.1)	25.5 (12.6 to 31.9)	0.1
Age (y)	2.5 (1.5 to 3.5)	3 (2.0 to 4.7)	0.04
Dogs with signs of active labor (%)	37	72	0.006

Table 2. Median (IQR) doses of anesthetic agents, duration of general anesthesia, incidence of hypotension defined as a MAP < 60 mmHg, frequency of use and dose of phenylephrine, and volume of crystalloids administered in dogs admitted for cesarean section between January 2014 and July 2018, either receiving an epidural injection or not. Dogs in the epidural group received bupivacaine 0.0625–0.125% with either fentanyl or buprenorphine.

	Epidural	Control	P-value
Propofol (mg/kg BW)	5 (4.0 to 6.0)	4.8 (3.1 to 6.0)	0.4
Alfaxalone (mg/kg BW)	2.1 (1.7 to 2.6)	1.3 (1.2 to 1.8)	0.04
Duration of anesthesia (min)	90 (75 to 108)	80 (65 to 105)	0.4
Average vaporizer setting/MAC	0.84 (0.8 to 0.9)	0.88 (0.82 to 1.05)	0.02
Incidence of hypotension (%)	81	62	0.1
Duration of hypotension (min)	5 (5 to 10)	5 (5 to 10)	0.4
Administration of phenylephrine (%)	81	62	0.1
Phenylephrine dose (μg/kg BW)	20 (10 to 30)	15 (10 to 60)	0.5
Volume of crystalloids (mL/kg BW per hour)	11 (8 to 16)	11 (7.5 to 17)	0.8
Extubation time (min)	5 (5 to 10)	5 (5 to 10)	0.9
Rectal temperature at extubation (°C)	37 (36.6 to 37.2)	37 (36.5 to 37.5)	0.7

BW — body weight; MAP — mean arterial pressure; MAC — minimum alveolar concentration.

bupivacaine was higher, if a different local anesthetic was used, or if the bitch received any sedatives or analgesics before induction of anesthesia. The only preanesthetic medication allowed for inclusion in the study were antiemetic and gastro-protectant agents, such as metoclopramide, maropitant, ondansetron, pantoprazole, and famotidine.

In each case, anesthesia was induced with IV propofol or alfaxolone and maintained with an inhalational agent in oxygen (2 to 3 L/min) and positive pressure ventilation. The electrocardiogram, pulse oximetry, capnography, and arterial blood pressures (either direct or oscillometric) were recorded throughout the procedure. All epidural injections were performed at the lumbosacral space using a Tuohy needle (22G to 18G, 2.0 to 3.5 inches; Perifix Tuohy Epidural Needle; B. Braun Medical, Pennsylvania, USA) with the dog under general anesthesia and in sternal recumbency. Either the hanging drop technique or the loss-of-resistance technique was used to identify penetration of the *ligamentum flavum.* Upon completion of surgery, a non-steroidal anti-inflammatory agent was administered after removal of the tracheal tube. Dogs were transferred to the care of the theriogenology service once mentation and analgesia were deemed adequate, signs of nausea were not detected, and motor function was present in the hind limbs, as assessed by the attending anesthetist. According to our hospital's practice, the puppies and dam were available for discharge within the first 2 h after surgery, providing that the puppies had nursed, and the bitch was ambulatory.

Retrospective data were abstracted from the patients' medical records. Dogs were divided into 2 groups: those receiving a low-dose bupivacaine epidural, and the control group. Among those dogs receiving an epidural injection, the concentration of bupivacaine, volume of solution per kg body weight (BW) injected by the epidural route, and addition of opioids to the epidural solution were recorded. If a midline infiltration was used in dogs in the control, this was also recorded.

For each dog, the age and weight were recorded, as well as whether signs of active labor were observed at presentation. The induction agent and dose used, and the type of inhalational agent were also recorded. The vaporizer setting throughout the procedure was recorded every 5 min and averaged and divided by the minimum alveolar concentration (MAC) for that agent in dogs [isoflurane: 1.28% (8), sevoflurane: 2.36% (9)]. Duration of anesthesia and time to extubate (from discontinuation of inhalational delivery to removal of the tracheal tube) were also recorded. Arterial hypotension was defined as a mean arterial pressure (MAP) < 60 mmHg; duration of such hypotension was recorded. The use of phenylephrine, opioids, or neuromuscular blocking agents was also recorded, as was the volume of crystalloid solution administered. The total number of puppies, and the percentage of live puppies delivered through surgery were also recorded.

Variables were compared between treatment groups with Fisher's exact test for categorical variables and Wilcoxon Rank Sum tests for numerical variables (JMP Pro 12.0.1; SAS Institute, Cary, North Carolina, USA). A value of $P < 0.05$ was considered significant. Results are summarized as median interquartile range (IQR).

A total of 66 records were analyzed; 37 dogs received an epidural injection and 29 did not. Eleven dogs in the control group received a line block before surgical incision. The median volume of solution injected by the epidural route was 0.2 mL/kg BW, (IQR: 0.17 to 0.22 mL/kg BW). Bupivacaine (Bupivacaine HCl 0.5%; Hospira, Lake Forest, Illinois, USA) was diluted with normal saline and an opioid to reach final concentrations of 0.0625% in 13 dogs, 0.1% in 4 dogs, and 0.125% in 20 dogs. Fentanyl (Fentanyl citrate; Akron, Lake Forest, Illinois, USA)

was used in 28 animals at a median dose of 4 μg/mL (IQR: 3 to 4 μg/mL) of epidural solution, and buprenorphine (Buprenex; Reckitt Benckiser Pharmaceuticals, Richmond, Vermont, USA) was administered to the remaining 9 dogs at a median dose of 4.6 μg/kg BW (IQR: 4.0 to 8.8 μg/kg BW). The median number of puppies delivered was 7 (IQR: 3 to 8) in the epidural group and 5 (IQR: 3 to 8) in the control group. Median percentage of puppies delivered alive was 100% (IQR: 86 to 100) in the epidural group and 100% (IQR: 81 to 100) in the control group (both $P > 0.2$).

The demographic characteristics of dogs are shown in Table 1. Variables pertaining to general anesthesia for each group are shown in Table 2.

Intraoperative opioids were administered to 18% of dogs in the epidural group and to 93% of dogs in the control group ($P < 0.0001$). In the epidural group, 5 dogs received methadone 0.1 to 0.3 mg/kg BW and 2 received fentanyl, 2 to 5 μg/kg BW, IV. One dog receiving fentanyl was also administered buprenorphine, 0.01 mg/kg BW, IV during recovery. Of the 29 dogs in the control group, 14 received buprenorphine (median: 0.02 mg/kg BW; IQR: 0.01 to 0.03 mg/kg BW), IV, 7 received methadone (median: 0.18 mg/kg BW; IQR: 0.1 to 0.2 mg/kg BW), IV, 5 received fentanyl (median: 3 μg/kg BW; IQR: 2 to 5 μg/kg BW), IV, and 1 received hydromorphone, 0.1 mg/kg BW, IV. All 11 dogs in the control group receiving a line block also received an intraoperative IV opioid. Buprenorphine was given after extubation to 5 dogs and methadone to 3 dogs in the control group. Neuromuscular blocking agents were administered to 43% of dogs in the epidural group and 72% of dogs in the control group ($P = 0.01$). Eight of the 11 dogs receiving a line block were also administered a neuromuscular blocking agent.

The main conclusions from this retrospective study were that the use of a low-dose bupivacaine epidural with either fentanyl or buprenorphine was associated with a reduction in the requirements for intraoperative analgesics and that the incidence of arterial hypotension was not augmented.

Epidural anesthesia with low doses of local anesthetics such as bupivacaine or ropivacaine, also referred to as "walking epidural," is commonly used to alleviate labor pain in women. This technique provides pain relief while minimizing motor block. A concentration-dependent effect on motor function was demonstrated with bupivacaine in awake dogs (10), and effective analgesia with minimal impact on motor function using bupivacaine 0.167% combined with morphine was shown in dogs undergoing laparotomy (11). Our results suggest that a further reduction in the concentration of bupivacaine preserves beneficial analgesic effects, as bupivacaine 0.0625–0.125% combined with an epidural opioid, reduced the use of intraoperative opioids.

The dogs received either fentanyl or buprenorphine as part of the epidural injections. Both agents have previously been used by this route: epidural buprenorphine has been shown to be effective after orthopedic surgery in dogs (12). Fentanyl has also been used epidurally in dogs, most commonly dosed on a μg/kg BW basis (13). Our service adopted a dosing modality often used in humans, whereby fentanyl is dosed in μg/mL of epidural solution (7).

The reduction in inhalational agents in the epidural group, while statistically significant, was clinically negligible. While our vaporizers are evaluated yearly for accuracy, end-tidal concentrations of anesthetic agents were not recorded; therefore, only vaporizer settings can be reported. We chose to normalize the average vaporizer setting through the entire procedure over the MAC of each agent in order to compare MAC multiples, since both sevoflurane and isoflurane had been used. Given the intrinsic error of this variable, and the small difference found between groups, it is likely that this statistical difference does not translate into an important clinical one.

No differences were found between groups in the incidence of hypotension, the duration of hypotension, the frequency of use of phenylephrine or its dose, and volume of fluids administered. These observations also suggest that the use of low concentrations of epidural bupivacaine combined with an opioid did not negatively affect arterial pressure when combined with inhalational anesthetics.

Once the puppies had been delivered, and before interruption of general anesthesia, almost all dogs in the control group had received intraoperative opioids. Due to the retrospective nature of this study, specific signs that prompted the anesthetists to administer intraoperative opioids cannot be discerned, yet it was surmised that medication was needed to palliate nociception or prevent postoperative pain. This was the case even in those dogs receiving a line block before abdominal incision, which suggests that at least in this population, local infiltration of the midline was insufficient to blunt signs of nociception. Almost 20% of the dogs receiving an epidural injection also received systemic opioids, suggesting that in those cases the epidural injection was either not successfully delivered, or that the epidural medication was insufficient to blunt nociception. Similarly, neuromuscular blockers were administered more often to dogs in the control group, likely due to a perceived insufficient muscular relaxation, or to control ventilation. Taken together, the increased use of inhalational agents, opioids, and neuromuscular blockers in the control group, suggests that the use of low-dose epidural anesthetic had a noticeable effect as an adjunct to general anesthesia in these dogs.

Although not analyzed in this study, a reduction in the use of systemic opioids by the administration of low-dose epidural bupivacaine could also improve the quality of the recovery period. The use of systemic opioids is often accompanied by sedation (14) and nausea (15); such side effects might negatively affect the overall comfort of the bitch in the early postoperative period. Similarly, time to ambulation after this combination of epidural agents merits further research. A prospective study investigating the quality and times of recovery and discharge after cesarean section is underway.

There are limitations to this study due to its retrospective nature. The anesthetists were not blinded to treatments. Small, albeit statistically significant, differences were found in the age of dogs and the dose of alfaxalone used between groups. More dogs in the control group were admitted with signs of active labor than those in the epidural group. It is likely that in some cases, active labor prompted the anesthetist to avoid the epidural injection in order to expedite the procedure.

In summary, the use of an epidural injection with bupivacaine 0.0625–0.125% in combination with either buprenorphine or fentanyl substantially reduced the use of systemic opioids and did not exacerbate arterial hypotension in dogs undergoing cesarean section under inhalational anesthesia.　　CVJ

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